

## Complexity of Retinoid Pathways Highlights Hans Falk Lecture

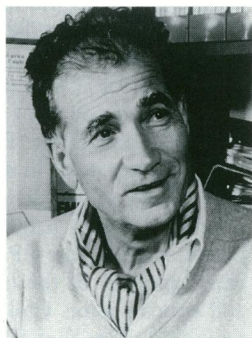
The complexity of retinoid functions in the body, and the pioneering research to identify them, was the subject of the eleventh Hans Falk Memorial Lecture presented December 7 at the NIEHS by Pierre Chambon, director of the Institut de Genetique et de Biologie Moleculaire et Cellulaire des Eucaryotes in Illkirch, France, which is associated with the National Center of Scientific Research.

Retinoids, retinoid metabolites, and synthetic derivatives of vitamin A play an important role in vertebrate development and cellular differentiation. The action of retinoids are mediated by specific receptors in the nucleus of cells. Six different genes have been reported to be involved in the action of retinoids. Excess of retinoids as well as interruption of the retinoid signaling pathways can lead to abnormalities in development and birth defects. Retinoid signaling pathways also play a crucial role in postnatal and adult life. For example, the maintenance of several epithelia as well as spermatogenesis are dependent on the presence of retinoids.

Genetically modified mice in which the expression of specific retinoid receptors have been eliminated or "knocked-out" have provided interesting models to determine the function of retinoid receptors. Some of these knock-out mice exhibit normal development and health, suggesting that some retinoid pathways are not critical to survival or that alternate systems are in place to compensate for missing retinoid pathways. Knock-out of a certain combination of retinoid receptors does appear to cause specific defects in development, indicating the complexities of the regulation of gene expression during development.

Chambon is internationally recognized for his scientific contributions on understanding the regulation of gene expression in eukaryotic cells, in particular the role of nuclear proteins in the cloning of the estrogen receptor. Recently, Chambon's laboratory has widened the field of retinoid research by identifying and characterizing retinoid receptors. This work has provided fundamental insights into the mechanisms of retinoid action and has spurred retinoid research in laboratories around the world.

The Hans L. Falk Memorial Lecture series



Pierre Chambon

features scientists who have made distinguished contributions to research related to environmental health sciences. Falk (1919-1985) was an internationally known environmental health science expert and one of the first scientific staff members at the NIEHS. Before joining the NIEHS, Falk served as associate scientific director for carcinogenesis at the National Cancer Institute.

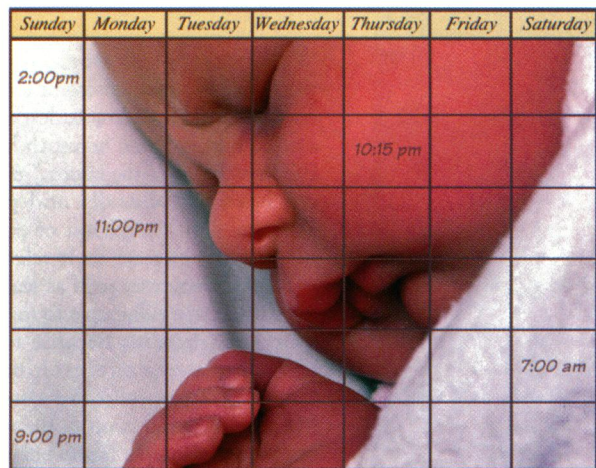
## Window of Opportunity

Sex every day seems to be best—at least for couples who are trying to get pregnant, according to the findings of a study by researchers at the NIEHS. The study, reported in the December 7 issue of the *New England Journal of Medicine*, revealed that pregnancy results from intercourse before ovulation, but not after ovulation, as was previously believed. "Couples who wait until ovulation to have intercourse may be missing their best chances for pregnancy," said Allen Wilcox, chief of the NIEHS Epidemiology Branch and co-author of the study with NIEHS researchers Clarice Weinberg and Donna Baird.

According to Wilcox, the six days ending on the day of ovulation seem to be the time when intercourse produces pregnancy. Until now, scientists have estimated the length of a woman's fertile period—the days on which conception can occur—to be as few as two days or as many as ten. In light of the new data, "Intercourse each day or every other day leading up to ovulation appears to be optimum" for achieving pregnancy, says Wilcox. The findings also provide valuable information to couples attempting to avoid pregnancy through the "rhythm method" of predicting ovulation.

The findings are the result of almost 10 years of testing and statistical analysis of data, from a four-year study begun in 1982, that included detailed diaries of intercourse kept by 221 women in North Carolina collated with tests of 27,000 urine samples taken daily from the same women. Scientists at Atlanta University performed the tests for steroid hormones in urine that signal the day of ovulation. Researchers at Columbia Uni-

versity used a new and highly sensitive assay to detect human chorionic gonadotropin (hCG) to identify implantation of a fertilized egg in the womb. NIEHS researcher Weinberg developed the statistical methods to show which day's intercourse was the likeliest to have produced the sperm that resulted in a particular conception.



**Missed conceptions?** New research shows conception occurs on the six days ending on the day of ovulation.

During the study, participants had 192 pregnancies, all of which resulted from sex either on the day of ovulation or one of the five preceeding days. According to the findings, the probability of pregnancy ranged from one in ten on the fifth day prior to ovulation to one in three on the day of ovulation. None of the pregnancies occurred even one day after ovulation, although the reason for this is unclear. "The rapid drop in the probability of conception after ovulation," said the study authors, "suggests a short survival time for ova, or perhaps a change in the cervical mucus after ovulation that obstructs the entry of new sperm."

The study also debunked two popular myths about conception. Although many physicians have advised against daily intercourse on the theory that it might decrease chances for conception by depleting the number or quality of sperm per ejaculation, the study found that intercourse every day is slightly more likely to produce conception than intercourse every other day. In addition, although authors of several recent books have asserted that intercourse timed with ovulation is more likely to produce male offspring, the NIEHS scientists found that timing of intercourse has no influence on the gender of offspring.